CACNA1C gene

calcium voltage-gated channel subunit alpha1 C

Normal Function

The *CACNA1C* gene belongs to a family of genes that provide instructions for making calcium channels. These channels, which transport positively charged calcium atoms (calcium ions) into cells, play a key role in a cell's ability to generate and transmit electrical signals. Calcium ions are involved in many different cellular functions, including cell-to-cell communication, the tensing of muscle fibers (muscle contraction), and the regulation of certain genes.

The calcium channel produced from the *CACNA1C* gene is known as CaV1.2. These channels are found in many types of cells, although they appear to be particularly important for the normal function of heart and brain cells. In the heart, CaV1.2 channels open and close at specific times to control the flow of calcium ions into cardiac muscle cells. By changing the electrical properties of these cells, calcium channels signal the cardiac muscle to contract and help maintain the heart's normal rhythm. The channels' role in the brain and in other tissues is less clear.

Researchers have discovered that many different versions of the CaV1.2 channel can be produced from the *CACNA1C* gene by a mechanism called alternative splicing. This mechanism produces different versions of the channel by cutting and rearranging the genetic instructions in different ways. Some versions of the CaV1.2 channel are more common than others in certain parts of the body. For example, in the heart and brain, about 80 percent of CaV1.2 channels are made with a particular segment known as exon 8. The other 20 percent of CaV1.2 channels contain a slightly different version of this segment, known as exon 8A. This difference becomes important when researchers are studying the effects of *CACNA1C* mutations in various tissues.

Health Conditions Related to Genetic Changes

Brugada syndrome

Timothy syndrome

Mutations in the *CACNA1C* gene are responsible for all reported cases of Timothy syndrome. One mutation has been found in everyone diagnosed with classic, or type 1, Timothy syndrome. This mutation changes one protein building block (amino acid) used to build the channel. Specifically, the mutation replaces the amino acid glycine with the amino acid arginine at position 406 (written as Gly406Arg or G406R).

The mutation that causes classic Timothy syndrome occurs in exon 8A, and is present only in the version of the CaV1.2 channel made with this segment. Therefore, in the brain and heart, the mutation affects about 20 percent of all CaV1.2 channels.

Two mutations in the *CACNA1C* gene cause a more severe, atypical form of Timothy syndrome called type 2. These mutations occur in the version of the CaV1.2 channel made with exon 8. One of these genetic changes, G406R, is the same mutation that causes classic Timothy syndrome when it occurs in exon 8A. The other mutation replaces the amino acid glycine with the amino acid serine at position 402 (written as Gly402Ser or G402S).

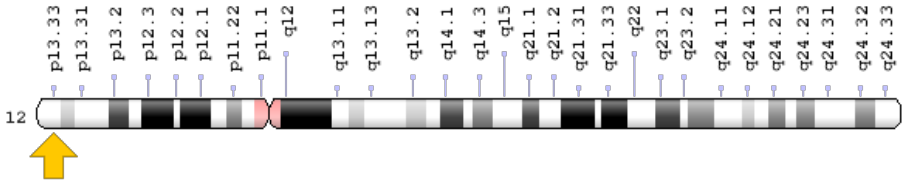
Because the mutations responsible for atypical Timothy syndrome occur in exon 8, they are present only in versions of the CaV1.2 gene that contain this segment. In the brain and heart, this version accounts for about 80 percent of all CaV1.2 channels. Researchers believe that the more severe features of atypical Timothy syndrome result from the higher percentage of mutated channels in heart and brain cells.

Mutations in the *CACNA1C* gene change the structure of CaV1.2 channels throughout the body. The altered channels stay open much longer than usual, which allows calcium ions to continue flowing into cells abnormally. The resulting overload of calcium ions within cardiac muscle cells changes the way the heart beats and can cause arrhythmia. Researchers are working to determine how an increase in calcium ion transport in other tissues, including cells in the brain, underlies the other features of Timothy syndrome.

Chromosomal Location

Cytogenetic Location: 12p13.33, which is the short (p) arm of chromosome 12 at position 13.33

Molecular Location: base pairs 1,969,677 to 2,697,949 on chromosome 12 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CAC1C_HUMAN
- CACH2
- CACN2
- CACNL1A1
- calcium channel, cardic dihydropyridine-sensitive, alpha-1 subunit
- calcium channel, L type, alpha 1 polypeptide, isoform 1, cardic muscle
- calcium channel, voltage-dependent, L type, alpha 1C subunit
- CaV1.2
- CCHL1A1
- DHPR, alpha-1 subunit
- MGC120730
- voltage-dependent L-type calcium channel alpha 1C subunit
- voltage-gated calcium channel alpha subunit Cav1.2

Additional Information & Resources

Educational Resources

- Eurekah Bioscience Collection: High Voltage-Activated Ca2+ Channels
  https://www.ncbi.nlm.nih.gov/books/NBK6181/#A30865
- Neuromuscular Disease Center, Washington University
  http://neuromuscular.wustl.edu/mother/chan.html#ca

GeneReviews

- Timothy Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1403

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28CACNA1C%5BTIAB%5D%29+OR+%28CaV1.2%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- CALCIUM CHANNEL, VOLTAGE-DEPENDENT, L TYPE, ALPHA-1C SUBUNIT
  http://omim.org/entry/114205

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_CACNA1C.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CACNA1C%5Bgene%5D
- HGNC Gene Family: Calcium voltage-gated channel subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/253
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=1390
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/775
- UniProt
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